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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,639	HE ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,32,34,36 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,32,34,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 31, 32, 34 and 36-37 are all the pending claims for this application.

2. New claims 36 and 37 were added in the Response of 2/21/07, and which find support in the originally filed specification and have priority to U.S. provisional application 60/509,350 (filed 10/4/02). Claim 31 was amended.

3. The amendments to the specification filed in the Preliminary Amendment of 2/6/04 to cross-reference the related priority applications and in the second Preliminary Amendment of 8/12/04 to introduce sequence identifiers has been considered and entered.

4. Claims 31, 32, 34 and 36-37 are all the claims under examination.

Withdrawal of Objections

Sequence Compliance

5. The objection to the Sequence Listing is withdrawn in view of Applicant's assurances that the CRF and paper copy are the same as filed with the "Communication Under 37 C.F.R. § § 1/821-1.825 and Preliminary Amendment" on 8/12/04, and further in view of Applicant's comments on p. 6, ¶2 of the Response of 2/21/07.

Specification

6. The objection to the specification for containing an embedded hyperlink and/or other form of browser-executable code (page 9, line 30, and page11, line 1) is

withdrawn in view of the amendments to the specification set forth on pp. 2-3 of the Response of 2/21/07. Applicant's comments on p. 6, ¶3 of the Response of 2/21/07 are acknowledged.

Withdrawal of Rejections

Claims - 35 USC § 112, second paragraph

7. The rejection of Claims 31, 32, and 34 under 35 U.S.C. §112, second paragraph, for Claim 31 reciting "a Dvl protein" is withdrawn in view of the amendment of Claim 31 to recite "Dvl-3", and further in view of Applicant's comments on pp. 6, ¶4- p. 7, ¶2 of the Response of 2/21/07.

Claims - 35 USC § 112, first paragraph

Written Description

8. The rejection of Claims 31, 32 and 34 under 35 U.S.C. §112, first paragraph, as failing to provide written support for the genus of agents against the genus of Dvl-3 proteins, more especially, those agents which inhibitor Dvl-3 expression is withdrawn in view of the amendment of Claim 31 to the species of Dvl-3 protein. Further, Applicant's explanation on pp. 9-11 of the Response of 2/21/07 detailing the written support for Dvl-3 expression inhibitors in the originally filed specification and as known in the art is considered persuasive.

Enablement

9. The rejection of Claims 31, 32 and 34 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for treating any cancer with any agent inhibiting expression of any Dvl protein is withdrawn in view of the amendment of Claim 31 to recite a method for inhibiting Dvl-3 expression in a cancer cell. Applicant's comments on pp. 11-15 of the Response of 2/21/07 have been considered and are found persuasive. Further, the references (Elbashir et al.; Elbashir et al.; Harborth et al.; and Semizarov et al. on p. 13 of the Response) cited by Applicant's in support of the art status for inhibiting cancer cell growth with siRNA at the time of application filing, have been considered and entered.

New Grounds for Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 31 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Song et al. (J. Biol. Chem. 275:23790-23797 (2000)).

Claims 31 and 37 are drawn to a method of inhibiting cancer cell growth for a cancer cell over-expressing Dvl-3 protein comprising contacting the cell with an agent for inhibiting Dvl-3 expression, and where the cancer cell is a breast cancer cell.

Song discloses that protein kinase C2 is postulated to be involved in tumorigensis where its activity is elevated solid tumors, transformed cell lines and rapidly proliferating tissues, and specifically when transgenically expressed, it promotes lymphoma and breast cancer (p. 23790, Col. 2). Song teaches that CK2 is important in modulating phosphorylation of Dvl-3 which is expressed in human breast mammary cells, because in contacting breast cells with an inhibitor of CK2, apigenin, the phosphorylation of Dvl-3 protein is diminished (Figure 5). Song teaches that apigenin reduces the levels of Dvl-3 protein in breast cells (Figure 6). Song teaches that

apigenin inhibits cell proliferation and causes G2/M arrest (Figure 3). Because the claims are not limited to the inhibition of Dvl-3 expression directly resulting in the inhibition of cancer cell growth, Song reads on and therefore anticipates the claims.

11. Claims 31, 32, 34 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Alsobrook et al. (US 20030229016; published December 11, 2003; priority to 8/26/02 and earlier).

The interpretation of Claims 31 and 37 is discussed supra. Claims 32 and 34 are drawn to a lung cancer cell and the agent being siRNA.

Alsobrook discloses methods for treating a cancer cell such as a lung cancer, breast cancer amongst other cancers [0016] using an siRNA [0080] which inhibits expression of a splice variant of a dishevelled-3-like protein (Table 1). Because the claims are not limited to any kind of Dvl-3 protein moiety, the species of a splice variant for a Dvl-3-like protein and methods for inhibiting the expression of the protein to inhibit cancer cell proliferation as disclosed by Alsobrook, read on and therefore anticipate the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 31 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al. (J. Biol. Chem. 275:23790-23797 (2000)) further in view of Bui et al. (Biochem. Biophys. Res. Comm. 239:510-516 (1997)).

The interpretation of Claims 31 and 37 is discussed supra. Notably, Claim 31 encompasses any kind of cancer cell.

The method of inhibiting breast or colon (amongst others such as leukemias, lymphomas, bladder cancers, endometrial cancers, etc.) cancer cell proliferation with agents that effect Dvl-3 expression was prima facie obvious at the time of the invention over Song in view of Bui.

The interpretation of Song is discussed supra. Song does not disclose Dvl-3 expression in the cancer cell lines in Table 1 of Bui.

Bui discloses Dvl-3 expression in various human cancer cell lines (breast and colon amongst several others) and that Dvl-3 is involved in signal transduction for epithelial tissues.

One skilled in the art would have been motivated and would have been reasonably assured of success in producing the method for inhibiting Dvl-3 expression in a cancer cell line in order to inhibit cancer cell growth based on the combined disclosures of Song and Bui. Song discloses the role of Dvl-3 in kinase signaling for breast cancer cells, and the success in using the kinase inhibitor, apigenin not only to block phosphorylation of the Dvl-3 substrate but to diminish the protein levels following cell contact with the agent, with the resultant effect of inhibiting cell proliferation. Because of the success achieved by Song and the evidence that apigenin had a direct or indirect effect on Dvl-3 protein levels in mediating inhibition of cancer cell proliferation, one skilled in the art would have been reasonably assured of success in extrapolating the method of Song to the treatment of other cancer cells such as those disclosed in Bui, because Bui teaches specific expression of Dvl-3 protein in these cancer cell lines.

Thus, for all of the foregoing reasons, the claims were prima facie obvious at the time of the invention over Song and Bui.

13. Claims 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al. (J. Biol. Chem. 275:23790-23797 (2000)) as applied to claim 31 above, and further in view of Engelmann et al. (Phytomedicine 9(6):489-495 (2002) Abstract).

The interpretation of Claims 31 and 32 is discussed supra.

The method of inhibiting lung cancer cell proliferation with agents that effect Dvl-3 expression was prima facie obvious at the time of the invention over Song in view of Engelmann.

The interpretation of Song is discussed supra. Song does not teach using the method of inhibiting cancer cell growth in a lung cancer cell. Engelmann rectifies this deficiency in its disclosure.

Engelmann discloses inhibiting lung cancer, glioma and colon cancers in vivo with apigenin and that inhibition of tumor blood vessel growth was weak but effective whereas intratumoral necrosis was elevated. Each of the cancer cell lines was reported to have also been sensitive to apigenin in vitro.

One skilled in the art would have been motivated and would have been reasonably assured of success in producing the method for inhibiting Dvl-3 expression in a lung cancer cell line in order to inhibit cancer cell growth based on the combined disclosures of Song and Engelmann. Song discloses the role of Dvl-3 in kinase signaling for epithelial cells such as breast cancer cells, and the success in using the kinase inhibitor, apigenin not only to block phosphorylation of the Dvl-3 substrate but to diminish the protein levels following cell contact with the agent, with the resultant effect of inhibiting cell proliferation. Because of the success achieved by Song and the

evidence that apigenin had a direct or indirect effect on Dvl-3 protein levels in mediating inhibition of cancer cell proliferation, one skilled in the art would have been reasonably assured of success in extrapolating the method of Song to the treatment of lung cancer cells such as those disclosed in Engelmann, because Dvl-3 protein expression would have been inherent to these cancer cell lines.

Thus, for all of the foregoing reasons, the claims were prima facie obvious at the time of the invention over Song and Engelmann.

14. Claims 31 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al. (J. Biol. Chem. 275:23790-23797 (2000)) as applied to claim 31 above, and further in view of You et al. (Proc. Am. Assoc. Cancer Res. 42: 609 (2001)) as evidenced by Uematsu et al. (Oncogene 22:7218-7221 (2003)).

The interpretation of Claim 31 is discussed supra. Claim 36 is drawn to a mesothelioma cell.

The method of inhibiting mesothelioma cell proliferation with agents that effect Dvl-3 expression was prima facie obvious at the time of the invention over Song in view of You

The interpretation of Song is discussed supra. Song does not teach using the method of inhibiting cancer cell growth in a mesothelioma. You rectifies this deficiency in its disclosure.

You (as evidenced by Uemtasu on p. 7218 (Col. 2, ¶2)) discloses that overexpression of Dvl, is a dominant event in mesothelioma, and it appears to induce tumorigenicity by a canonical Wnt signaling pathway.

One skilled in the art would have been motivated and would have been reasonably assured of success in producing the method for inhibiting Dvl-3 expression in a mesothelioma cell in order to inhibit cancer cell growth based on the combined disclosures of Song and You. Song discloses the role of Dvl-3 in kinase signaling for epithelial cells such as breast cancer cells, and the success in using the kinase inhibitor, apigenin not only to block phosphorylation of the Dvl-3 substrate but to diminish the protein levels following cell contact with the agent, with the resultant effect of inhibiting cell proliferation. Because of the success achieved by Song and the evidence that apigenin had a direct or indirect effect on Dvl-3 protein levels in mediating inhibition of cancer cell proliferation, one skilled in the art would have been reasonably assured of success in extrapolating the method of Song to the treatment of mesothelioma cells such as those disclosed in You (as evidenced by Uemtasu), because Dvl-3 protein expression was disclosed as being directly tumorigenic in mesothelioma cells.

Thus, for all of the foregoing reasons, the claims were prima facie obvious at the time of the invention over Song and You (as evidenced by Uemtasu).

15. Claims 31 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alsobrook et al. (US 20030229016; published December 11, 2003; priority to 8/26/02 and earlier) in view of in view of You et al. (Proc. Am. Assoc. Cancer Res. 42: 609 (2001)) as evidenced by Uematsu et al. (Oncogene 22:7218-7221 (2003)).

The interpretation of Claim 31 is discussed supra. Claim 36 is drawn to a mesothelioma cell.

The method of inhibiting mesothelioma cell proliferation with agents that effect Dvl-3 expression was prima facie obvious at the time of the invention over Alsobrook in view of You

The interpretation of Alsobrook is discussed supra. Alsobrook does not teach using the method of inhibiting cancer cell growth in a mesothelioma. You rectifies this deficiency in its disclosure.

The interpretation of You (as evidenced by Uemtasu on p. 7218 (Col. 2, ¶2)) is discussed supra.

One skilled in the art would have been motivated and would have been reasonably assured of success in producing the method for inhibiting Dvl-3 expression in a mesothelioma cell in order to inhibit cancer cell growth based on the combined disclosures of Alsobrook and You. Alsobrook discloses methods for inhibiting cancer cell proliferation with agents such as siRNA that effect expression of a splice variant for a Dvl-3-like protein in cancer cells, and the success in using the siRNA to diminish the protein levels following cell contact with the agent, with the resultant effect of inhibiting cell proliferation. Because of the success achieved by Alsobrook and the evidence that

siRNA had a direct or indirect effect on Dvl-3 protein levels in mediating inhibition of cancer cell proliferation, one skilled in the art would have been reasonably assured of success in extrapolating the method of Alsobrook to the treatment of mesothelioma cells such as those disclosed in You (as evidenced by Uemtasu), because Dvl-3 protein expression was disclosed as being directly tumorigenic in mesothelioma cells.

Thus, for all of the foregoing reasons, the claims were prima facie obvious at the time of the invention over Alsobrook and You (as evidenced by Uemtasu).

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

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SUPERVISORY PATENT EXAMINER